

REMARKS

Applicants note there appears to have been an inadvertent error in claim numbering. Claims 1-44 were present in the application as originally filed. Claims 1-36 were cancelled and new claims, incorrectly numbered as 37-46, were submitted in the response filed March 18, 2005. To avoid confusion, Applicants herein have cancelled claims 1-46 without prejudice to continued prosecution in a continuation application and submit new claims 47-53. Claims 47-49 generally correspond to incorrectly numbered claims 37 and 42-43.

Support for claim 47 can be found, e.g., at page 21, line 4, and page 25, lines 1-2 and 28-30.

Support for claim 48 can be found, e.g., at page 15, lines 7-8, page 22, line 10 and at page 40, lines 2-3.

Support for claim 49 can be found, e.g., at page 15, lines 7-8 and at page 22, line 10.

Support for claims 50-53 can be found, e.g., at page 22, line 10 and page 40, lines 2-3.

Applicants have inserted the word "SephadexTM" at page 15, line 4, to clarify it is SephadexTM G-150 that is referred to in this sentence.

No new matter has been added. Accordingly, claims 47-53 are pending.

Applicants thank the Examiner for the courtesy of a personal interview on August 30, 2005. Amendments to claims 37 and 42-43 were discussed and Applicants remarks below regarding the § 112 and § 102/103 rejections were discussed. A sample of crosslinked dextran beads on gauze was shown at the interview.

In light of the amendments and the remarks herein, Applicants respectfully request reconsideration and allowance of the pending claims.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 40 and 41 under 35 U.S.C. § 112, second paragraph as indefinite for reciting what the Examiner considered to be trademarks. In order to further prosecution and without prejudice to continued prosecution in a continuation application,

Applicants have herein cancelled claims 40 and 41, thereby rendering the rejection moot. Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 37-39 and 42-46 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner stated that the limitation of "cross-linked polysaccharide beads" wherein the beads are "starch, alginate, or cellulose," did not have support in the specification as filed.

Applicants respectfully disagree. In order to further prosecution, however, and without prejudice to continued prosecution in a continuing application, new claim 47 recites cross-linked dextran beads, an embodiment which the Examiner acknowledged is supported by the present specification. Applicants have also cancelled claims 39-41 without prejudice. Accordingly, Applicants respectfully request withdrawal of the rejection with respect to new claims 47-53.

The Examiner also asserted that claims 41 and 42 lacked written description, as the Examiner asserted that HP-15 or HP-20 were not disclosed "in the environment of a dry removable wound dressing wherein the gauze matrix has a coating of cross-linked polysaccharide beads." Applicants believe that the Examiner intended to refer to dependent claims 40-41. Applicants have cancelled these claims without prejudice in order to further prosecution, thereby rendering the rejection moot. Applicants respectfully request withdrawal of the rejection.

The Examiner also rejected claims 43-44, asserting that the molecular weight exclusion limits recited in claims 43-44 were based exclusively on two proprietary products, HP 15 or HP 20, the source and availability of which could not be determined. Applicants believe that the Examiner intended to refer to dependent claims 42-43.

Applicants respectfully submit that the exclusion limits recited in new claims 48-53 are based exclusively on products whose source and availability can be determined. It is stated in the specification at page 15, lines 4-6, that

HP 15 means 1 gram of G-150 that swells 15 times its original volume when placed in an aqueous environment. Its molecular weight exclusion limit is 3×10^5 or greater.

"G-150" is a well-known mark for Sephadex™ crosslinked dextran beads, as shown by Downstream Thirty, a copy of which is included in the attached Information Disclosure Statement. G-150 is readily available to those of ordinary skill. Second, the recited materials are available to one of ordinary skill simply by making them in a laboratory. It is stated in the specification at page 40, lines 1-5, that

[d]ry spheres or beads were prepared by cross-linking dextran (MS 65,000 – 70,000) with epichlorohydrin. The resulting crossed-linked dextran had exclusion limits of 100,000 MW to 300,000 MW depending on the degree of cross-linking.

It is also stated in the specification at page 40, lines 14-15, that

[d]ry spheres or beads were prepared by cross-linking dextran (MW 65,000-70,000) with epichlorohydrin. The resulting crossed-linked dextrans had a exclusion limit of 300,000 MW.

In view of the specification, it is clear that cross-linked dextran beads are readily available to one having ordinary skill, simply by cross linking dextran (MW 65,000-80,000) with epichlorohydrin to achieve the desired molecular weight exclusion limit, e.g., 1×10^5 , 3×10^5 , 5×10^5 , or 6.5×10^5 . Accordingly, it is clear that one of ordinary skill would have recognized that Applicants were in possession of the invention as claimed in new claims 48-53. The Examiner is respectfully requested to withdraw the rejection for lack of written description with respect to these claims.

Finally, the Examiner rejected claim 46, asserting that no support could be found in the specification for the recitation of mixtures of pharmaceutical agents. In order to further prosecution, Applicants have herein cancelled claim 46 without prejudice, thereby rendering the rejection moot. Applicants respectfully request withdrawal of the rejection.

Double Patenting Rejections

The Examiner provisionally rejected claims 37-43 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 72-84 of copending Application No. 10/334,864 (Attorney Docket No. 14004-005001). The Examiner asserted that the claims in each of the applications are directed to substantially the same subject matter.

Applicants respectfully disagree, but nonetheless request the Examiner to hold the rejection in abeyance with respect to the new claims pending an indication of such claims are otherwise allowable.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 37 and 39 under 35 U.S.C. § 102(b) as being anticipated by Eagles *et al.*, (U.S. Patent No. 5,840,777) ("Eagles"). In particular, the Examiner stated that Eagles discloses a gauze coated with cross-linked alginate. The Examiner presumed that beads are present at least to some extent.

The Examiner rejected claims 37-39, 44, and 46 under 35 U.S.C. § 102(b) as being anticipated by Patel (U.S. Patent No. 5,470,576) ("Patel"). As with Eagles, the Examiner stated that Patel discloses a gauze coated with cross-linked alginate. The Examiner presumed that beads are present at least to some extent.

The Examiner also rejected claims 37-39, 44, and 46 under 35 U.S.C. § 102(b) as being anticipated by Johnson & Johnson (UK Patent No. 629,419) ("J&J"), similarly stating that J&J discloses cross-linked alginate on gauze. The Examiner presumed that beads are present at least to some extent.

Applicants respectfully disagree. A claim is anticipated only if each and every limitation is disclosed in a single prior art reference. *See, e.g., Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 639 (Fed. Cir. 1989) and MPEP § 2131. "To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Company USA, Inc. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 7435 (Fed. Cir. 1999).

Present claim 47 recites a dry, removable wound dressing comprising a gauze matrix having a coating of cross-linked dextran beads on the gauze matrix. In contrast, none of the cited references disclose a gauze matrix having a coating of cross-linked dextran.

Eagles et al. discusses the formation of a foam from polysaccharides such as alginate, hyaluronate, carrageenans, chitosan, starch, amylose and amylopectin. Eagles et al. at column 2, line 62 to column 3, line 1. Applicants have found no mention of dextran in Eagles et al.

Patel discusses that the steps for making a dressing having 100% calcium alginate or a mixture of sodium alginate and calcium alginate. Patel at column 5, lines 43-56 and column 6, lines 18-30. Applicants have found no mention of dextran in Patel.

J&J discusses a dressing having alginic acid or a mixture of alginic acid and calcium alginate. J&J at page 1, lines 61-69. Applicants have found no mention of dextran in J&J.

In view of the above, Applicants respectfully submit that none of the cited references anticipate the present claims. Accordingly, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. § 102(b) over the Eagles, Patel, or J&J references.

Rejection under 35 U.S.C. § 103(a)

The Examiner also rejected claims 37-44 and 46 under 35 U.S.C. § 103(a) as being unpatentable over Johnson & Johnson or Patel taken with G.B. 1454055 (“’055”) and Smith (U.S. Patent No. 3,671,280) (“Smith”). In particular, the Examiner asserted that each of J&J and Patel discloses a gauze coated with cross-linked alginate. The Examiner also asserted that ‘055 discloses a gauze wound dressing comprising dextran beads, and that Smith teaches a gauze matrix coated with a composition comprising high-molecular weight dextran. The Examiner concluded that it would have been obvious to one having ordinary skill in the art to modify the gauze coated with cross-linked alginate polysaccharide as taught by J&J or Patel by substituting a cross-linked polysaccharide such as dextran as taught by ‘055 and Smith for the benefit of obtaining a dry, removable wound dressing that is pliable and easily removable and which has hemostatic properties.

Applicants respectfully traverse with respect to the pending claims. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested

to those of ordinary skill in the art that they should make the claimed composition, and (2) whether the prior art would also have revealed that in so making, those of ordinary skill would have had a reasonable expectation of success. *See, e.g., In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Applicants agree with the Examiner that neither of the primary references disclose cross-linked dextran beads. Office Action at page 7, lines 1-2. However, Applicants respectfully disagree that combining either of the primary references with the secondary references, '055 and Smith, renders the present claims patentably obvious. Applicants will first discuss the '055 reference, followed by the Smith reference.

The '055 reference contains no specific suggestion and provides no motivation for one of ordinary skill to substitute cross-linked dextran for cross-linked alginate in the compositions of J&J or Patel. The '055 reference is generally directed to compositions for cleansing skin surfaces. *See, e.g., GB '055* at page 1, lines 9-19 and lines 40-41; page 2, lines 36-38 and lines 43-47; page 7 lines 8-15, lines 62-73, lines 85-98; page 8, lines 22-27, lines 108-111; and page 9, lines 16-19. The '055 reference hypothesizes that coagulation at a discharging skin surface is modified or stopped by the gel formed from dextran particles, but is moved to a zone remote therefrom. *GB '055* at page 2, lines 43-47 and lines 86-92. It was thought that the participation of fibrinogen in scar formation took place in this zone, remote from the skin surface. *GB '055* at page 2, lines 71-75. The reference further hypothesizes that "[c]leansing of the discharging surface is facilitated by keeping the discharging surface free from coagulation, thereby also facilitating granulation development." *GB '055* at page 2, lines 93-97. Applicants respectfully submit that the statements and hypotheses in the *GB '055* reference teach away from substituting dextran for alginate in the compositions of the primary references, because one of ordinary skill would have understood that "stopping coagulation" at a skin surface, moving fibrinogen away from a discharging skin surface and keeping the skin surface "free from coagulation" is exactly the opposite of the effect desired when making a wound dressing that stops bleeding.

The '055 reference contains no disclosure of a gauze wound dressing having cross-linked dextran beads sprayed as a layer onto a wound-contacting surface of said gauze matrix. The '055 reference refers to material mixed with, or incorporated in, fibrous materials such as

cellulose fibers or paper pulp. GB '055 at page 6, lines 69-79. Gauze is woven, however, in contrast to fibrous materials such as cellulose fibers or paper pulp. See, American Heritage Dictionary of the English Language, page 752 (Houghton Mifflin, 1992) in the attached IDS. '055 also discusses material enclosed between layers of paper, cotton fabric or inert plastics, and states that the fabric "must, of course, have such a mesh size that particles cannot pass through the meshes" GB '055 at page 6, lines 101-106. Gauze is loosely woven, however, and cannot prevent particles from passing through the meshes of the gauze. The '055 reference discusses applying cross-linked dextran beads to a skin sore, and then covering the sore with a gauze bandage. See, GB '055 at page 7, lines 8-28. It is apparent that cross-linked dextran beads were not sprayed as a layer on the gauze bandage. The '055 reference also indicates that when crosslinked dextran particles and paper pulp were mixed, the paper pulp fibres were uniformly distributed between the crosslinked dextran particles. GB '055 at page 8, lines 33-65. It is apparent that crosslinked dextran beads were mixed with paper pulp and were not sprayed as a layer on a gauze matrix. In view of the above, the '055 reference does not disclose cross-linked dextran beads sprayed as a layer onto a wound-contacting surface of a gauze matrix.

In addition, Applicants note that so-called "secondary" considerations such as failure of others must be given due weight by the Examiner during *ex parte* prosecution. In re Sernaker, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983). Here, there has been a failure of others to appreciate the usefulness of a gauze matrix sprayed with a layer of cross-linked dextran beads. The '055 reference was published in 1976; cross-linked dextran beads have been known since the 1960s. See, e.g., Downstream Thirty, Amersham Pharmacia Biotech (1999) in the attached IDS. Yet, none of the hemostatic wound dressings disclosed in the articles in the attached IDS are made of cross-linked dextran beads sprayed on gauze. Pusateri et al., J. Trauma 55:518-526 (2003); Sondeen et al., J. Trauma 54:280-285 (2003); Crosseal™ Fibrin Sealant (2003); and Tisseel™ VH Fibrin Sealant Product Label (2003). The use of components other than crosslinked dextran beads in current hemostatic wound dressings is evidence that those of ordinary skill have failed to appreciate the hemostatic properties of cross-linked dextran beads sprayed as a layer on gauze.

The mere fact that references can be combined does not render a claimed invention patentably obvious unless the cited art suggests the desirability of the combination. In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Here, the cited references, alone or combined, do not specifically teach or suggest the desirability of the invention as presently claimed.

Finally, even if it is assumed that the references provide motivation, one of ordinary skill in the art would have had no reasonable expectation of success in substituting the dextran beads of '055 for the alginate materials of the primary references. The hypotheses in '055 regarding moving fibrinogen away from a discharging skin surface and keeping the skin surface free from coagulation, discussed above, would have created considerable uncertainty for one of ordinary skill and would not have given a reasonable expectation of success that substituting dextran for alginate would have made a successful hemostatic wound dressing. In fact, one having ordinary skill in the art might have expected that crosslinked dextran beads would stop coagulation, based on the statements in the '055 reference.

The Smith reference is similarly deficient. Smith discloses plaster of Paris compositions that can include high molecular weight dextran for, *e.g.*, for improving the strength and moisture resistance of casts. In determining whether art is analogous in an obviousness rejection, it must be determined (1) whether the reference is within the field of the inventor's endeavor; and (2) if not, whether the reference is reasonably pertinent to the particular problem with which the inventor was involved. *See In re Deminski*, 796 F.2d 436 (Fed. Cir. 1986). The claimed invention and a reference can be in the same field of endeavor if they have essentially the same function and structure. *Id.* Smith is thus non-analogous art, as the preparation of plaster of Paris casts is not reasonably pertinent to the preparation of hemostatic wound dressings, and the claimed invention and the reference (plaster of Paris casts) do not have essentially the same function and structure. Thus, while a plaster of Paris cast is useful to set broken bones, one having ordinary skill would not have expected that plaster of Paris technology is relevant to compositions designed to stop bleeding.

Moreover, even if Smith were analogous art, Smith provides no teaching or suggestion that one having ordinary skill in the art should modify the compositions of the primary references to include cross-linked dextran beads. At most Smith suggests that one of ordinary

skill should use high molecular weight dextran, which is not cross-linked dextran beads. In addition, the plaster of Paris casts of Smith provide no expectation whatsoever that substituting dextran for the cross-linked alginate of the primary references would have resulted in hemostatic wound dressings.

The '055 and Smith references taken together further support the patentability of the pending claims. One of ordinary skill, presented with either of the primary references and both the '055 and Smith references, would not have been motivated to substitute dextran, whether crosslinked ('055) or non-crosslinked (Smith) in the primary references, for the reasons discussed above. The lack of a reasonable expectation of success based on each reference alone would have been compounded when the two references are considered together.

Consequently, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) in view of J&J or Patel taken with GB '055 and Smith be withdrawn.

The Examiner also rejected claim 45 under 35 U.S.C. § 103(a) in view of various references. Applicants have herein cancelled claim 45, thereby rendering the rejection moot.

Applicant : Kent Cochrum et al.
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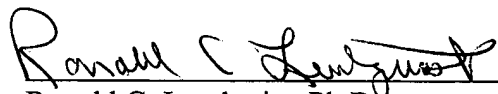
CONCLUSION

Applicants respectfully assert that all claims are in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned attorney if such would expedite prosecution.

Enclosed is \$60.00 check for the Petition for Extension of Time fee (1 month), along with a Supplemental Information Disclosure Statement. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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